08mar03 15:29:01 User208600 Session D1563.1

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(MU OR M) (W) CONOTOXIN **Items Description**

RD (unique items) STRIATUS 2279

CONOTOXIN 1 S2 AND S3 5449

S3 AND S5 9

ID (sorted in duplicate order)

'S3(W)2' OR 'S32 S3(W)2 OR S32 8

S5 AND S10

(Item 1 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2003 BIOSIS. All rts. reserv. 10345420 BIOSIS NO.: 199698800338

Scorpion toxins affecting sodium current inactivation bind to distinct homologous receptor sites on rat brain and insect sodium

AUTHOR: Gordon Dalia(a); Martin-Eauclaire Marie-France; Cestele Sandrine; Kopeyan Charles; Carlier Edmond; Khalifa Rym Ben; Pelhate Marcel; Rochat Herve

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JOURNAL: Journal of Biological Chemistry 271 (14):p8034-8045 1996 ISSN: 0021-9258 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

As specific probes for rat and insect sodium channels, we used the radiolabeled alpha-scorpion toxins. AaH II and Lqh-alpha-IT, the most active alpha-toxins on mammals and insect, respectively. We demonstrate that the different scorpion toxins may inactivation and toxic to mammals, with alpha-scorpion toxin receptor sites on both mammalian and insect sodium channels. ABSTRACT: Sodium channels possess receptor sites for many neurotoxins, of which several groups were shown to inhibit sodium current inactivation. Receptor sites that bind alpha- and alpha-like scorpion toxins are of particular interest since neurotoxin binding at these extracellular regions can affect the inactivation process at intramembranal segments of the be classified to several groups, according to their in vivo and in vitro activity on mammalian and insect sodium channels. channel. We examined, for the first time, the interaction of different scorpion neurotoxins, all affecting sodium current

<u>a</u> alpha-mammal scorpion toxins, and the anti-insect Lqh-alpha-IT bind to homologous but not identical receptor sites on both rat binding interactions with other scorpion toxins suggest the presence of a putative additional receptor site on sodium channels, the presence of a cluster of receptor sites for scorpion toxins that inhibit sodium current inactivation, which is very similar on which may bind a unique group of these scorpion toxins (Bom III and IV), active on both mammals and insects. We suggest Analysis of competitive binding interaction reveal that each group may occupy a distinct receptor site on sodium channels. scorpion toxins, is suggested to bind to a partially overlapping receptor site with both AaH II and Lqh-alpha-IT. Competitive brain and insect sodium channels. Sea anemone toxin ATX II, previously considered to share receptor site 3 with alphainsect and rat brain sodium channels, in spite of the structural and pharmacological differences between them. The sea anemone toxin ATX II is also suggested to bind within this cluster

7/6/1 (Item 1 from file: 5) 07872222 BIUSIS NU.: ขบบบระเวเลงเลง ALPHA CONOTOXINS SMALL PEPTIDE PROBES OF NICOTINIC ACETYLCHOLINE RECEPTORS 1991

Calcium channel subtypes in rat brain: biochemical characterization of the high-affinity receptors for omega-conopeptides SNX-230 (synthetic MVIIC), SNX-183 (SVIB), and SNX-111 (MVIIA). Aug 1994

(Item 2 from file: 155) 08345224 95103030 PMID: 7804605

7/6/4 (Item 4 from file: 5) 13357882 BIOSIS NO.: 200100565031 delta- Conotoxin structure/function through a cladistic analysis. 2001

Delta-conotoxin structure/function through a cladistic analysis. Nov 6 2001

(Item 3 from file: 155) 12598876 21540680 PMID: 11683628

Effects of ibogaine and noribogaine on phosphoinositide hydrolysis. 1996 (Item 5 from file: 5) 10583622 BIOSIS NO.: 199699204767

7/6/6 (Item 6 from file: 5) 06280311 BIOSIS NO.: 000086114494
PHYLOGENETIC SPECIFICITY OF CHOLINERGIC LIGANDS ALPHA CONOTOXIN SI 1988

Phylogenetic specificity of cholinergic ligands: alpha-conotoxin Sl. Sep 6 1988 7/6/7 (Item 7 from file: 155) 05978702 89062448 PMID: 3196703

7/6/8 (Item 8 from file: 5) 10348684 BIOSIS NO.: 199698803602 Neuroactive peptides of the marine snail, Conus striatus. 1996 7/6/9 (Item 9 from file: 5) 09798202 BIOSIS NO.: 199598253120 Veuroactive peptides of the marine snail, Conus striatus. 1995 7/6/10 (Item 10 from file: 155) 07476923 93003172 PMID: 1390774

Novel alpha- and omega-conotoxins from Conus striatus venom. Oct 20 1992

(Item 11 from file: 5) 08744594 BIOSIS NO.: 199395033945

Novel alpha- and omega-conotoxins from Conus striatus venom. 1992

A new conotoxin affecting sodium current inactivation interacts with the delta- conotoxin receptor site. Jan 20 1995 (Item 12 from file: 155) 08393950 95138099 PMID: 7836370

A new conotoxin affecting sodium current inactivation interacts with the delta-conotoxin receptor site. 1995 (Item 13 from file: 5) 09672271 BIOSIS NO.: 199598127189

A new family of Conus peptides targeted to the nicotinic acetylcholine receptor. 1995 7/6/14 (Item 14 from file: 5) 10071539 BIOSIS NO.: 199598526457

7/6/15 (Item 15 from file: 155) 08004758 94132020 PMID: 8300586

A new neurotoxin receptor site on sodium channels is identified by a conotoxin that affects sodium channel inactivation in molluscs and as an antagonist in rat brain. Jan 28 1994

A New Neurotoxin Receptor Site on Sodium Channels Is Identified by a Conotoxin That Affects Sodium Channel Inactivation in Molluscs and Acts 7/6/16 (Item 16 from file: 5) 09173865 BIOSIS NO.: 199497182235 as an Antagonist in Rat Brain. 1994

7/6/17 (Item 17 from file: 155) 10039018 99036623 PMID: 9819194 An O-glycosylated neuroexcitatory conus peptide. Nov 17 1998 (Item 18 from file: 5) 10345420 BIOSIS NO.: 199698800338

Scorpion toxins affecting sodium current inactivation bind to distinct homologous receptor sites on rat brain and insect sodium channels. 1996

(Item 19 from file: 5) 12614201 BIOSIS NO.: 200000367703 Solution structure of alpha-conotoxin St. 2000 (Item 8 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2003 BIOSIS. All rts. reserv. 10348684 BIOSIS NO.: 199698803602

Neuroactive peptides of the marine snail, Conus striatus

AUTHOR ADDRESS: Marine Sci. Inst., Univ. Philippines, Quezon City** Philippines

JOURNAL: Journal of Natural Toxins 5 (1):p122 1996

CONFERENCEMEETING: 209th American Chemical Society National Meeting on Natural Toxins Anaheim, California, USA April 2, 1995-April 7, 1996 ISSN: 1058-8108 RECORD TYPE: Citation LANGUAGE: English

(Item 9 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2003 BIOSIS. All rts. reserv 09798202 BIOSIS NO.: 199598253120

Neuroactive peptides of the marine snail, Conus striatus.

AUTHOR: Cruz L J

AUTHOR ADDRESS: Marine Sci. Inst., Univ. Philippines, Diliman, Quezon City **Philippines

JOURNAL: Abstracts of Papers American Chemical Society 209 (1-2):pAGFD 19 1995

CONFERENCE/MEETING: 209th American Chemical Society National Meeting Anaheim, California, USA April 2-6, 1995 SSN: 0065-7727 RECORD TYPE: Citation LANGUAGE: English

77/17 (Item 17 from file: 155) DIALOG(R)File 155:MEDLINE(R) (c) format only 2003 The Dialog Corp. All rts. reserv. 10039018 99036623 PMID: 9819194

An O-glycosylated neuroexcitatory conus peptide.

Craig A G; Zafaralla G; Cruz L J; Santos A D; Hillyard D R; Dykert J; Rivier J E; Gray W R; Imperial J; DelaCruz R G; Sporning A; Terlau H; West P J; Yoshikami D; Olivera B M

The Clayton Foundation Laboratories for Peptide Biology, The Salk Institute, San Diego, California 92186-5800, USA. Biochemistry (UNITED STATES) Nov 17 1998, 37 (46) p16019-25, ISSN 0006-2960 Journal Code: 0370623 Contract/Grant No.: GM48677; GM; NIGMS Document type: Journal Article Languages: ENGLISH

Main Citation Owner: NLM Record type: Completed

We purified and characterized a novel peptide from the venom of the fish-hunting cone snail Conus striatus that inhibits voltage-gated K+ channels. The peptide, kappaA- conotoxin SIVA, causes characteristic spastic paralytic symptoms when injected into fish, and in frog nerve-muscle preparations exposed to the toxin, repetitive action potentials are seen in response to a single stimulus applied to the motor nerve. Other electrophysiological tests on diverse preparations provide evidence that is consistent with the peptide blocking K+channels. The peptide has three disulfide bonds; the locations of Cys residues indicate that the spastic peptide may be the first and defining member of a new family of Conus peptides, the kappaA-conotoxins, which are structurally related to, but pharmacologically distinct from, the alphaA-conotoxins. This 30 AA tricyclic toxin has several characteristics not previously observed in Conus peptides. In addition to the distinctive biological and physiological activity, a novel biochemical feature is the unusually long linear N-terminal tail (11 residues) which contains one O-glycosylated serine at position 7. This is the first evidence for O-glycosylation as a posttranslational modification in a biologically active Conus peptide. Record Date Created: 19981217

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L13 NCCNGGCSSK/SQSP

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L21 L1

L2ANSWER 1 OF 1 CA COPYRIGHT 2003 ACS

AN 136:146437 CA

New members of the .mu.-conotoxin family for use in the treatment of disease associated with sodium channel function and cDNAs encoding them

IN Olivera, Baldomero M.; McIntosh, J. Michael; Garrett, James E.; Watkins, Maren; Cruz, Lourdes J.; Shon, Ki-Joon; Jacobsen, Richard; Jones, Robert M.; Cartier, G. Edward; Shen, Gregory S.

PΑ University of Utah Research Foundation, USA; Cognetix, Inc.

SO PCT Int. Appl., 231 pp.

CODEN: PIXXD2

DT Patent LĄ English

FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE --------------PΙ WO 2002007678 A2 20020131 WO 2001-US23125 20010723 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2001082945 A5 20020205 AU 2001-82945 20010723 PRAI US 2000-219619P Р 20000721 US 2000-245157P Ρ 20001103 US 2001-264319P P 20010129 US 2001-277270P Р 20010321 WO 2001-US23125 W 20010723

AB The present invention is to .mu.-conopeptides, derivs. or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivs. thereof and pharmaceutically acceptable salts thereof for the treatment of disorders assocd. with voltage-gated sodium channels. Thus, the .mu.-conopeptides or derivs. are useful as neuromuscular blocking agents, local anesthetic agents, analgesic agents and neuroprotective agents. The .mu.-conopeptides are also useful for treating neuromuscular disorders. The invention is further directed to nucleic acid sequences encoding the .mu.-conopeptides and encoding propeptides, as well as the propeptides.